CLINICAL PROFILE AND RISK FACTORS OF ENURESIS IN CHILDREN

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CERTIFICATE

This is to certify that the dissertation entitled "**CLINICAL PROFILE AND RISK FACTORS OF ENURESIS IN CHILDREN"** is the bonafide work of **Dr.S.P.KARAMATH** in partial fulfillment of the requirements for **M.D.(Paediatrics) Branch – VII** Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in March 2010.

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DECLARATION

I, **DR.S.P.KARAMATH**, solemnly declare that dissertation titled, "**CLINICAL PROFILE AND RISK FACTORS OF ENURESIS IN CHILDREN**" is a bonafide work done by me at The Institute of Social Paediatrics, Govt. Stanley Medical College & Hospital during 2007 – 2010 under the guidance and supervision of **DR.M.L.VASANTHAKUMARI, M.D., D.C.H.,** Director , Institute of Social Paediatrics and **DR.SUJATHA SRIDHARAN, M.D., D.C.H.,** and **DR.G.KARUNAKARAN, M.D., D.C.H.,** Professors, Institute of Social Paediatrics, Stanley Medical College, Chennai – 600 001.

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Introduction

Enuresis is a common problem, which may lead to important psychosocial sequalae. It can affect 5-18% of children in different age groups. It is well-known that enuresis is a common, genetically complex and heterogeneous disorder among children. Enuresis is multifactorial & several pathophysiological mechanisms have been proposed, including bladder dysfunction, a small functional bladder capacity, abnormal nyctohemeral vasopressin levels, nocturnal polyuria, and abnormal sleep patterns and arousability.

Lower urinary tract function and malfunction in children is a field rife with semantic confusion. Different groups use different definitions of commonly used terms, such as enuresis, incontinence, Overactive Bladder (OAB). The International Children's Continence Society (ICCS), which is the global multidisciplinary organization for professionals involved with the pediatric Lower Urinary Tract, has come with standardization of terminologies.

This study was undertaken to assess for the etiological riskfactors in enuresis in this part of the country and also to compare the risk factors in enuresis subgroups.

Review of Literature

Enuresis is defined as repeated, spontaneous voiding of urine during sleep in a child five years or older. Enuresis may be classified as primary or secondary, and monosymptomatic (uncomplicated) or nonmonosymptomatic (i.e., concomitant lower urinary tract symptoms are present). *Table 1* summarizes the types of enuresis.

Nocturnal enuresis is three times more common than daytime wetting. It occurs three times more often in boys. Secondary causes account for less than 20 percent of cases.

The history of nocturnal enuresis[1]

Ebers papyrus, the first document to address enuresis, found in Luxor 3,500 years ago, revealed that mothers and children used to take medicines made from water plants, suggesting that enuresis had a familial nature. Thirty-five centuries afterwards, Guyon brought up the family incidence of enuresis. At the time of Greek Romans, Aristotle, a follower of Plato, was the first to reflect upon the causes of enuresis by observing children's difficulty in waking up from sleep.

During the Renaissance, Paulus Begellardus drew up the first treaty on pediatric medicine which, in its 20th chapter, affirmed that "parents get particularly irritated when their children wet the bed regularly, sometimes

way into the pubertal stage...". In 1544, Thomas Phaer, the father of Pediatrics in England, recommended several therapies that consisted of powdered rooster windpipe, bladder from animals, intestine and brain from mice, in the chapter "Bedwetting" of his work Boke of Chyldren.

Guersent (1815) described the hereditary factor, higher incidence among boys and in economically-underprivileged social classes, and the effect of enuresis on children's mind, by referring to enuresis as "an aspect of sadness and shame that also affected their intelligence". The bladder was considered to be the determinant factor for enuresis due to the weakness, irritability, and lack of sensitivity attributed to it. This conception originated two forms of treatment: one for stimulating and another for slowing down bladder activity. In the late 19th century, galvanic or faradic current discharges used to be gently applied on the entire genital region of enuretic children. Technical reports on this technique became available all over the world, and Hernamann-Johnson, in the early 20th century, said that "the simplest method consists in introducing a metallic plug into the bladder and discharge the electric current up to the children's limit of tolerance". Trousseau and his followers preached the use of soothing therapy, especially one that was based on the belladonna, a plant that became very popular during a long time. Other hypotheses such as small sized bladder, defective bladder neck, defective trigone and urethral meatus with reduced sensitivity led to new treatment options such as bladder distension with fluids, insufflated vaginal rings in order to constrict the bladder neck, cauterization with silver nitrate to sensitize the urethra, and bedwetting aids that kept a 45

angle between trunk and hips.

Guersent was the first to describe relative nocturnal polyuria; only hundreds of years after that, Poulton and Hinden brought this hypothesis to light again, which did not arouse any interest until 1980, when researchers found out that enuretic children produced less anti diuretic hormone (ADH) during the night.

Scolding and punitive attitudes that attacked children's self-esteem were recommended for "simulators", and urethral occlusive devices such as the one invented by Wilks, which consisted of a velvet-covered iron tube shaped like a boy's penis, or that created by Labat, which had the advantage of leaving circulation free within the cavernous bodies, were used.

In the 20th century, three events remarkably changed the history of enuresis: alarm therapy, imipramine and desmopressin.

Development of vesicourethral sphincter control

Soon after birth, urination occurs spontaneously as a medullary reflex. From the first year of life onwards, two important events take place: increase in bladder capacity and neural maturation of frontal and parietal lobes. The cortical command produces the sensation of bladder filling; however, neurological maturity to initiate or inhibit urination is not present yet. The complete maturity with voluntary control of external

vesicourethral sphincter and ability of cerebral cortex to initiate or inhibit detrusor contraction occurs only later. This allows children to control urination and defecation, adjusting them according to socially defined patterns.

At the age of five, 85% of children have total vesicourethral control, while the remaining 15% become continent at an annual rate of 15%. At the pubertal stage, 2 to 5% continue to be enuretic, and in adulthood, this rate is approximately 1.5 to 3%.[2,3]

Definitions

The word enuresis originated from Greek and means “wetting oneself”. Therefore, it defines socially unacceptable urinating behavior. Nocturnal enuresis means urinating during sleep. Since it is a unique symptom after the habitual age at which children learn to control urination, enuresis is considered monosymptomatic, and presupposes normal functioning of the nervous and urinary systems or absence of other well-defined organic conditions as causative agent. If nocturnal enuresis is associated with other symptoms, it is considered polysymptomatic.

The International Children’s Continence Society (ICCS) has published standards of terminology and definitions for the symptoms, investigative tools, diagnosis and treatments pertinent to children with nocturnal enuresis and other forms of voiding dysfunction[4].

The definitions are listed below:

Enuresis:

Intermittent incontinence of urine while sleeping, i.e. synonymous with (Intermittent) Nocturnal Incontinence. The term is used regardless of whether daytime incontinence or other lower urinary tract symptoms is also present. Nocturnal may be added for extra clarity.

Monosymptomatic Enuresis:

Enuresis in a child without any (other) lower urinary tract symptoms.

Non Monosymptomatic Enuresis:

Enuresis in a child with (Other) Lower urinary tract symptoms, such as daytime incontinence, urgency, holding maneuvers etc.,

Primary Enuresis:

Enuresis in a child who has never attained continence or has been previously been dry for less than 6 months

Secondary Enuresis:

Enuresis in a child who has previously been dry for at least 6 months.

Epidemiology

The accuracy of data on the prevalence of Enuresis is currently hampered by the lack of standardized criteria for the selection of patients, in addition to the influence of geographic, social and cultural factors. The literature presents an Enuresis prevalence rate of 3 to 22% at the age of seven, and 0.4 to 8.4% at the age of ten. Usually, this rate remains around 10% at the age of seven.[1]

Enuresis is more frequent in boys up to the age of ten years who belong to lower social classes; the incidence of Enuresis is incontestably influenced by genetic factors. After the age of ten, the frequency is the same for both boys and girls.

Pathogenic factors

1) Genetic factors

Enuresis is a development disorder whose hereditary component has a heterogeneous character, described since 1890, which involves parents, brothers and sisters and other close relatives, and increases the probability of enuresis by 2 to 6 times. Children whose mother and father have previous history of enuresis present 77% of chances to suffer from this disorder, and if only one parent used to be enuretic, the chances amount to 44%; however, if there is no previous parental history of enuresis, the chances drop to15 %[2].

Molecular biology seems to have a better explanation to the genetic transmission of enuresis. Genes found on chromosomes 12q, 13q and 8q

seem to be involved.

2) Delay of the circadian rhythm of antidiuretic hormone (ADH)

The amount of ADH in the bloodstream, secreted by the posterior pituitary gland, is reduced soon after birth and, after one year, ADH levels equal those presented by adults. ADH levels usually increase during the night, resulting in reduced urine volume. A disorder in the circadian rhythm of ADH causes increased urine production, exceeding bladder capacity and explaining enuresis, although it does not explain why children do not wake up from sleep when the bladder is full.

3) Sleep and wakefulness

There has been an attempt to define the correlation of enuresis with different sleep stages; however, results have been inconclusive. Parents usually report that their enuretic children have deep sleep, showing a tendency towards wakening difficulty or inability to recognize the sensation of bladder filling during sleep. The reason for this wakening dysfunction may be related to immature thalamic function.

4) Bladder capacity and uninhibited detrusor contractions

Small bladder capacity has been described as an Enuretic etiologic agent. The limited number of urodynamic studies in enuretic children and the nonstandardized selection of patients cast doubt on the interpretation of results. No significant difference has been effectively determined so far.

If there is more than one enuretic event on the same night and higher frequency of diurnal urination, or in cases that are refractory to all forms of treatment, it is necessary to rule out possible bladder instability through the Urodynamic study. These children benefit from an anticholinergic treatment.

5) Psychological implications and nervous system

The idea that enuresis is a symptom of emotional stress has been replaced with the evidence that most enuretic children manifest secondary psychological disorders that affect their self-esteem; these children profit from early guidance and treatment.

6) Other factors

Intestinal constipation acts as a mechanical factor, preventing the bladder to expand to its full capacity. Other factors may correlate with enuresis, such as allergy to cow's milk, effects of caffeine or cocoa derivatives, airway obstruction (sleep apnea) or even nocturnal fluid overload (induced enuresis).

Clinical Features :

History :

The best time to investigate enuresis is when the parent or patient first raises the issue in the physician's office. However, the optimal time for treating enuresis should be based on the motivation of the child.

The history should include fluid intake, daytime voiding pattern, and number and time of episodes of bedwetting.

A sleep history should include the times the child goes to bed, falls asleep, and awakens in the morning. Parents should be asked to subjectively comment on the depth of sleep of the child. The presence of restless sleep, snoring, and the type and frequency of nocturnal arousals (eg, nightmares, sleep terrors, sleepwalking) should be determined.

Whether the child has experienced periods of dryness and the circumstances of these episodes should also be determined.

A diet history should include the timing, quantity, and type of fluid and solid food intake during the day and after supper.

An assessment of the emotional impact on the child is important. Information should be solicited from both the parents and the child. Basic and revealing information includes whether the child has experienced teasing by family or friends or has self-restricted participation in school, sleepovers, or trips.

Patients with overactive bladder or dysfunctional voiding usually present with frequency, urgency, squatting behavior, and daytime and nighttime wetting. Constipation and cystitis are common associated problems in patients with overactive bladder or dysfunctional voiding.

Symptoms of cystitis include dysuria; cloudy, foul-smelling urine; visible blood in the urine; frequency; urgency; and day and nighttime wetting. Symptoms of cystitis can be very subtle in some children.

Constipation manifests as infrequent and painful passage of hard wide stool, encopresis, and colicky periumbilical pain.

Symptoms of sleep disordered breathing (SDB) include snoring, mouth breathing, lack of restful sleep, and tiredness the following morning.

The hallmark symptoms of urethral obstruction are the need to wait or push to initiate voiding and a weak or interrupted stream.

When bedwetting is a feature of a major motor seizure, parents may hear nocturnal sounds associated with abnormal muscle movements.

Symptoms of diabetes mellitus include polyuria, polydipsia, and weight loss notwithstanding a voracious appetite.

Patients with diabetes insipidus present with polyuria, polydipsia, and symptoms related to the underlying hypothalamic or renal causes.

Physical Examination:

A comprehensive physical examination is important. The examination would include the following:

- Measurement of blood pressure
- Inspection of external genitalia
- Palpation in the renal and suprapubic areas to look for enlarged kidneys or bladder
- Thorough neurologic examination of the lower extremities, including gait, muscle power, tone, sensation, reflexes, and plantar responses.
- Inspection and palpation of the lumbosacral spine
- Abnormal physical findings are usually absent in children when enuresis is the sole symptom and are not necessarily present in children with overactive bladder or dysfunctional voiding.

Abnormal physical findings may be found in patients with cystitis, constipation, neurogenic bladder, urethral obstruction, ectopic ureter, obstructive sleep apnea (OSA), and hyperthyroidism.

Causes :

Idiopathic:

If no cause can be identified, the important pathophysiologic factors include a disorder of sleep arousal, nocturnal polyuria, and a low nocturnal bladder capacity.

Disorder of sleep arousal

Studies reveal that children with enuresis do not wake up normally in response to an auditory signal; these studies confirm a defect in arousal[5,6,7].

Arousal to the sensation of a full or contracting bladder involves interconnected anatomic areas, including the cerebral cortex, reticular activating system (RAS), locus ceruleus (LC), hypothalamus, pontine micturition center (PMC), spinal cord, and bladder. The RAS controls depth of sleep, the LC controls arousal, and the PMC initiates the command for a detrusor contraction. Various neurotransmitters are involved, including noradrenaline, serotonin, and antidiuretic hormone (ADH).

Nocturnal polyuria

Factors that cause nocturnal polyuria in children with enuresis include the following:

Fluid ingestion before bedtime

Food consumption before bedtime

Low nocturnal secretion of ADH

Increased nocturnal solute excretion

Excess intake of caffeine

Production of urine is controlled by several factors, including ADH, which directly controls water absorption, and atrial natriuretic peptide (ANP) and aldosterone, which control solute and, therefore, indirectly affect water

excretion.

Norgaard et al were the first to report absence of the expected nocturnal increase in ADH secretion in children with enuresis. Subsequent reports suggest that low nocturnal secretions of ADH are present in some but not all children with enuresis[1,8,9].

Low bladder capacity

Small functional bladder capacity is a long-suspected pathophysiologic factor for enuresis. The literature includes reports of normal and reduced functional bladder capacity, but few studies report on carefully selected patients with only enuresis[10].

In a study by Mattsson and Lindstrom, functional bladder capacity (FBC) was positively correlated with nighttime urine output. Children with enuresis possibly maintain a smaller nocturnal bladder volume, and this situation may condition the detrusor to contract at a lower volume[11].

Overactive bladder/dysfunctional voiding

Overactive bladder/dysfunctional voiding usually presents with urinary frequency, urgency, squatting behavior, daytime wetting, and enuresis.

Cystitis

Cystitis is a common cause of enuresis and an aggravating factor associated with other causes. Cystitis associated with enuresis might present at any age.

Cystitis causes uninhibited detrusor contractions that can lead to episodes of day and nighttime wetting.

If cystitis is the only cause of enuresis, other symptoms of infection are usually present, and the wetting resolves with an appropriate antibiotic.

Cystitis is more common in children with overactive bladder/dysfunctional voiding, neurogenic bladder, urethral obstruction, ectopic ureter, and diabetes mellitus. In these conditions, daytime symptoms do not resolve completely with antibiotic treatment.

Psychological causes

Various common situations predispose to a psychological cause, including birth of a new sibling, parental divorce or separation, a death in the family, child abuse, or any other cause of social dysfunction at home or school[12].

Constipation

Constipation can cause both PE and SE and is a common aggravating factor that should be considered when other causes are present.

Although the mechanism is not clear, the pressure effect of stool in the descending or sigmoid colon possibly can trigger an uninhibited detrusor contraction. Constipation is usually present in children with neurogenic bladder and is more common in those with overactive bladder and dysfunctional voiding.

Sleep disordered breathing

SDB is a disorder associated with both an abnormality in arousal and enuresis. The most common cause of SDB in childhood is adenotonsillar

hypertrophy.

The dramatic resolution of enuresis following surgical treatment of airway obstruction suggests SDB influences a critical pathophysiologic factor. A disorder of sleep arousal is suggested as the most likely factor.

Seizure disorder

SE may be a symptom of an unobserved overnight major motor convulsion in a child with a known seizure disorder.

New-onset seizures rarely occur only at night, and bedwetting is, therefore, a rare manifestation.

Ectopic ureter

This rare congenital abnormality is due to the insertion of the ureter in a location other than the lateral angle of the bladder trigone. Enuresis results when the insertion is distal to the external urethral sphincter.

Ectopic ureter is 3-4 times more common in girls than in boys and causes incontinence only in females.

Diabetes mellitus

Enuresis is usually not the presenting complaint in a child with new-onset diabetes mellitus. Conventional symptoms of insulin deficiency usually overshadow the presence of bedwetting.

Diabetes insipidus

Diabetes insipidus is an uncommon cause of enuresis. Although nocturnal polyuria is often presumed to be the cause of bedwetting, a disorder

of arousal may also be present.

Bladder Diary: Frequency-Volume and Bedwetting Charts

A bladder diary is an essential assessment tool in toilet trained children and includes recordings of daily fluid intake, urine output and bladder related symptoms at home under normal conditions. When properly filled-in, it should include data regarding the number of voidings per day, the distribution of voids during the day, the voided volume as well as records of any episodes of urgency and leakage. It is a useful tool to help identify underlying dysfunction and those who may warrant further studies as well as in followup.

As opposed to a freqency-volume chart, a bladder diary would also provide further information on nocturia, enuresis and incontinence episodes. The bedwetting chart would allow one to assess the severity of enuresis and to monitor progress.

Laboratory Investigations

Laboratory investigations are generally not routinely required unless the child presents with complications such as urinary tract infections. However, to complement a full workup, urinalysis may be performed to rule out bacteriuria and glucosuria. Early morning urine specific gravity may be looked at in cases of nocturnal enuresis to assess renal concentrating ability.

Ultrasonogram

An ultrasonogram (USG) is often the first-line investigation in children with non-neurogenic voiding dysfunction as it is a simple, readily available and

noninvasive tool which is able to provide information both on anatomical and functional problems when performed by experienced radiologists.

Other Imaging Studies

Radiological examination of the spine may be necessary to rule out any spinal malformations or other neurogenic causes of voiding dysfunction.

A micturating cystourethrogram may be performed in patients to rule out vesicoureteral reflux. Information on the bladder emptying efficiency may be obtained and the status of the urethra can be assessed to exclude any outflow obstruction.

Urodynamic Studies

Urodynamic studies (UDs) are employed to describe the physiological parameters involved in the bladder mechanics during filling and voiding. A complete study would involve cystometry combined with uroflowmetry and perineal electromyography (EMG). Bladder filling and storage can then be described according to bladder sensation, detrusor activity, bladder compliance and bladder capacity.

According to most protocols, UDs are reserved for those Children who don't improve in spite of therapy with behavior therapy/ alarm and pharmacotherapy[13].

Treatment

1) Treatment onset

Considering that Enuresis is a benign condition, its spontaneous resolution rate is approximately 15% per year, the placebo effect is high, and that there is a possibility of relapse after successful treatment, treatment regimens that are free from side effects are preferred. However, the effect on enuretic children's self-esteem is a good indicative sign that the matter deserves serious consideration.

The ideal age for treatment onset depends on each patient's individual condition, their maturation, and the level of family tolerance. General guidance may start before the age of 5, and drug or nondrug treatment may be implemented after the sixth year of life.

2) General Guidelines

Some preliminary guidelines and nonspecific actions should also be considered for children younger than 5 years old, discontinuation of diapers; maintenance of urinating schedules; bladder voiding before going to bed; perception of bladder filling; awareness of the ability to control the sphincter either to initiate or stop urination.

Among the major measures, we have: show children that Enuresis is very frequent and several schoolmates suffer from the same problem; try to remove guilt and motivate children; avoid excessive fluid intake at night,

eradicate any punitive attitudes, and provide positive support instead.

3) Alarm therapy

The first described device dates back to 1904, when a German physician designed a hospital mattress with a mechanism that indicated when nurses had to change the clothes of hospitalized children; some of the children did not wet the bed anymore after spending some time in that hospital.

The therapy yielded good results, approximately 50 to 70% on the medium and long run, with a reduction in the incidence of relapses between 0 and 30%; was also safe and simple to apply, and did not present side effects. But this is not widely replicated in clinical practice. The major reasons for this include lack of immediate results, cultural aspects, unavailability, form of commercialization,and lack of expertise.

The principle of alarm therapy is based upon the electrical conduction of urine. Every time involuntary urination occurs,a sound or vibratory mechanism is triggered, waking children up and having them cease urination. Children may not wake up immediately or just wake up during or after urination, gradually learning to anticipate or perceive urinary urge. Expected results are only achieved after at least 4 months of continued use.

This method depends a lot on motivation, that is, patients who will not mind waking up. Alarm therapy can only be used on children who are able to understand and control the device.

Some causes of treatment failure include unmotivation, early discontinuation, difficulty in waking up, night terror (children wake up and cannot sleep any longer), behavioral disorders, inadequate home environment, mother's anxiety, more than one nocturnal episode, low socioeconomic status.

6) Drug treatment[14,15]

a) Desmopressin acetate (DDAVP)

Desmopressin is structurally analogous to the antidiuretic hormone, which reduces the nocturnal production of urine.The 1-deamino-8-D-arginine-vasopressin molecule was synthesized in 1966. The deamination of N-terminal halfcysteine in position 1 causes an increase in antidiuretic activity and duration of action (10-12 hours) due to a higher action on V2 receptors of collecting duct cells. The replacement of L-arginine at position 8 with D-arginine is responsible for the reduction in the vasopressin activity, causing the action on V1 receptors of smooth muscle fibers to be almost nonexistent.

The efficiency and safe use of desmopressin in MNE has been described for over 20 years.Several literature reports show approximately 70% of total and/or partial response. The optimization of desmopressin use is based on parameters such as normal bladder capacity, patient's age, increased volume of nocturnal diuresis, and urinary osmolarity. The selection of cases,

whose pathogenic mechanism involved is relative insufficiency of nocturnal ADH secretion, may provide higher efficiency.

Desmopressin is available in nasal and oral solutions. Nasal desmopressin is the most widely used. Oral desmopressin is recommended for children with rhinitis or respiratory tract infections. Dosage equivalence for the nasal solution is 20 mg, and 200 mg, for the oral solution. The dosage may be reduced in 50% or doubled after 2 weeks, depending on the initial response, and maintained for 3-4 months, with later gradual reduction.

In the event of relapses, the regimen may be repeated or combination therapy (desmopressin + alarm) may be used. Another option for patients who present good response is to restrict the use of desmopressin to social events, at which enuresis must be avoided.

Desmopressin must be administered 1 hour before bedtime, and it is necessary that fluid intake be limited to 30 ml/kg, 2 hours before up to

12 hours after administration so that the risk for hyponatremia and even seizures secondary to water intoxication can be avoided. Some possible side effects are mild headache(2%), nasal congestion, rhinitis and epistaxis (1%), and abdominal pain (1%). Desmopressin must not be prescribed to children with polydipsia, high blood pressure, or heart disease.

b) Imipramine

Imipramine has gained widespread use since 1960, although its action mechanism is not clear, and is probably related to anticholinergic and sympathomimetic effects. The antidepressant effect does not seem to be involved, since other antidepressants show no effect on enuresis.The therapeutic result is nearly similar to that of desmopressin, also in terms of relapse episodes. The dosage ranges between 0.5 and 2.0 mg/kg/day, not exceeding 50 mg/day up to the age of 12 years and 75 mg/day after this age. Imipramine is administered in a single dose, approximately 2 hours before bedtime, and yields the desired results, that is, a reduction of over 50% in enuresis frequency.

After 2 weeks, the dosage may be readjusted or maintained for 3 to 6 months, and then gradually reduced until discontinuation is possible.

c) Anticholinergics

It is important to emphasize that there is no recommended use of anticholigernics for MNE. If bladder instability is confirmed through urodynamic investigation, we classify enuresis as a symptom of urination disorder, and a specific treatment protocol, including the use of anticholinergics, is recommended.

Aim of the study

To study the “clinical profile of children presenting with enuresis to a tertiary care hospital”

To compare the risk factors in Enuresis subgroups namely Primary versus Secondary enuresis and Monosymptomatic versus Nonmonosymptomatic enuresis.

Materials & Methods

This descriptive observational study was conducted in the Institute of Social Paediatrics, Govt. Stanley Hospital, Chennai. All children between the ages of 5 to 12 who presented to the OPD with the complaint (As a primary one or one of the many) of bedwetting constituted the study material.

DSM IV definition of enuresis was used for defining a case of enuresis .i.e.

Repeated involuntary or intentional voiding during the day or night in clothes or in bed

At least 2 such events per week for at least 3 consecutive months or the presence of clinically significant distress in social, academic or other important areas of functioning

Chronological age of at least 5 years or more

Children with developmental delay/ cerebral palsy or other manifest neurological disorder were excluded.

Detailed history of each child fulfilling above mentioned criteria was recorded in a preformed proforma and complete neurological examination was done. Lumbosacral spine was examined to look for nevus, dimple, gluteal folds asymmetry or tuft of hairs. Abdomen was palpated for distended bladder, kidneys and fecoliths.

All patients underwent urine analysis & culture, stool examinations for ova and cysts and X-ray Lumbosacral spine – AP and lateral view for spina

bifida occulta. Ultrasound abdomen was also done in each case for any renal/bladder wall changes and residual urine after voiding.

All patients were given a frequency – volume chart and asked to fill it up over 48 hours at home and the charts were collected back.

All children were sub classified as Primary/Secondary and the primary enuretics were sub classified into monosymptomatic/Non Monosymptomatic. The data were entered and analyzed using Epiinfo software. Chi-square tests with Yates correction wherever necessary and Fisher P tests (where numbers were small and chi-square could not be applied) were used to compare the groups.

Observation & Results

A total of 51 patients with enuresis presented during the study period. No parent or child refused to participate in the study. There were 30 males (58%) and 21 females (42%). Of the 51 children who were enuretic, 48 had only nocturnal enuresis (94%).No strict daytime enuresis was recorded. Combined daytime and nocturnal enuresis accounted for only 3 cases (6%). 84% of cases were primary (n=43) while only 16 % were secondary (n=8).

Table – 1 Age Group Distribution

Age Group	**All Case n=51 (%)**	**Primary n= 43(%)**	**Secondary n= 8(%)**	**Significance**	
				χ^2	**P value**
5-7 yrs	19 (37.3)	17 (39.5)	2 (25)	3.001	**0.2230**
8-10 yrs	19 (37.3)	17 (39.5)	2 (25)		
11-12 yrs	**13 (25.4)**	**9 (21)**	**4 (50)**		

The mean age at presentation was 8.75 years for all cases, for Males being 9.27 years and for females 8 yrs.

Sex Distribution:

There were 30 males and 21 females. Though males were higher in proportion among primary enuresis it was not statistically significant.

Table – 2 Sex Distribution

	Males (%)	**Females (%)**
Primary	26(60.5)	**17(39.5)**
Secondary	**4(50)**	**4(50)**

Some of the risk factors associated with enuresis are presented in the table below

Table – 3 Risk Factors for Enuresis

	Total (n)	**Percentages(%)**
Total No	51	
Males (%)	30	**58.8**
Females (%)	21	**41.2**
Daytime symptoms (any)	45	**88.2**
Storage symptoms	19	**43.1**
Bladder overactivity	26	**51**
Cystitis symptoms	5	**9.8**
Difficulty in arousal	27	**52.9**
Low Sp.Gravity	28	**54.9**
Spina Bifida	19	**37.25**
Low Bladder Capacity	26	**51**
Family History	21	**41.2**
Constipation	2	**3.9**

Documented UTI	3	**5.9**
Sleep disordered breathing	7	**13.7**
Low income	**31**	**60.78**

Spina Bifida Occulta:

Spina bifida occulta was found in 37.25 % of cases (n= 19) by X ray examination. The level of spina bifida was L5 in 6 cases, S1 in 8 cases and L5S1 in 5 cases.

Table – 4 Spina Bifida

Level of Spina Bifida	**No of Cases**
L 5	**6**
L5 S1	**5**
S 1	**8**

Family History:

Family history was present in 21 cases (41.18%). Majority of these children had history of enuresis in one parent (35 %) and 1 child had a sibling who was enuretic and 2 other children had both parents who were enuretic.

Table – 5 Family History

Family History	**No of Cases**
One parent	**18**
Both Parents	**2**
Sibling	**1**

Difficulty in arousability:

Children were assessed for arousability by Sleep arousal score (SAS). A score of 1 to 8 was assigned. Children who had a score of 1-3 were classified as easy to arouse, 4-5 as moderate and 6- 8 as difficult to arouse.

More than half (52 %) were found to have difficulty in arousability.

Small Bladder capacity:

Functional Bladder capacity was assessed using Frequency – volume charts as per ICCS guidelines. Maximal voided volume was noted and if it was within 65 % to 130 % of expected bladder capacity, the child was designated as having Normal Bladder capacity.

Expected Bladder capacity was calculated using the formula

Estimated Bladder capacity = (Age in Years x 30) + 30 in ml

Comparison of Primary Enuretics with Secondary Enuretics:

When compared both primary and secondary enuretics were similar in presentation except in storage symptoms, Cystitis symptoms and symptoms of sleep disordered breathing which were significantly higher in Secondary enuresis and low income which was more significant in primary enuresis.

Storage Symptoms:

Storage symptoms like increased day time frequency, daytime incontinence and nocturia were significantly more associated with secondary enuresis than primary (P = 0.0224)

Table – 6 Storage Symptoms

	Storage symptoms present	Storage symptoms not present	Significance	
			χ^2	P
Primary	13	30	4.026	***0.0448***
Secondary	6	2		

Symptoms of Bladder over activity:

Symptoms of bladder over activity like urgency and urge incontinence were the commonest daytime symptoms in enuresis (51 %, n= 21), there was not any significant difference between Primary and secondary enuresis. (P =0.4759)

Table – 7 Bladder Overactivity

	Bladder Overactivity present	Absent	Significance	
			χ^2	P
Primary	22	21	0.105	0.4759
Secondary	4	4		

Cystitis/UTI symptoms:

Symptoms of cystitis like dysuria, Lower abdominal pain, Hematuria were present in 5 cases though documented UTI was present only in 2 cases and cystitis symptoms were more in Secondary Enuresis which was also statistically significant. (P= 0.0132)

Table – 8 Cystitis Symptoms

	Cystitis symptoms present	Absent	Significance	
			χ^2	P
Primary	2	41	4.935	***0.0132***
Secondary	3	5		

Arousability:

Arousability was assessed using a sleep arousal score and children were classified into easily/Moderate/Difficult to arouse. Difficult to arouse were 52.9 % of study population.

Table – 9 Arousability

	Difficult to arouse	Moderate and Easy to arouse	Significance	
			χ^2	P
Primary	22	21	0.042	0.4191
Secondary	5	3		

Low Specific Gravity:

Early morning urine specific gravity was done and low specific gravity was noted as a risk factor since nocturnal polyuria due to defect in ADH secretion is a putative causal factor.

Low specific gravity was found in 54.9 % of patients (n =28)

Table – 10 Specific Gravity

	Low Specific Gravity	Normal specific Gravity	Significance	
			χ^2	P
Primary	24	19	0.007	0.3808
Secondary	4	4		

Spina Bifida Occulta:

As already observed spina bifida was present in 37.25 % of all children and there was no significant difference in the two groups.

Table – 11 Spina Bifida

	Spina Bifida Occulta present	Absent	Significance	
			χ^2	P
Primary	17	26	0.146	0.351
Secondary	2	6		

Bladder Capacity:

There was no significant difference in the two groups with regards to the bladder capacity.

Table – 12 Bladder Capacity

	Low Bladder Capacity	Normal Bladder Capacity	High Bladder capacity	Significance	
				χ^2	P
Primary	21	22	1	3.053	0.2173
Secondary	5	2	1		

Constipation:

Constipation was present in only 2 cases and there was no significant difference between the groups.

Table – 13 Constipation

	Constipation	No Constipation	Significance	
			χ^2	P
Primary	2	41	0.137	0.2669
Secondary	0	8		

UTI:

Documented UTI was present only in 3 cases.There was no significant difference between the two groups.

Table – 14 UTI

	UTI + (Culture positive)	No UTI (Culture Negative)	Significance	
			χ^2	P
Primary	2	41	0.002	0.4747
Secondary	1	7		

Family History:

There was no difference statistically in the presence of family history.

Table – 15 Family History

	Family History present	No Family History	Significance	
			χ^2	P
Primary	19	24	0.386	0.2672
Secondary	2	6		

Sleep Disordered Breathing (SDB):

Symptoms of sleep disordered breathing such as snoring, Mouth Breathing or increased sleepiness in the day were associated with secondary enuresis.(P value < 0.0001)

Table – 16 Sleep Disordered Breathing

	SDB present	No sleep disorderd breathing	Significance	
			χ^2	P
Primary	2	41	14.490	***0.0001***
Secondary	5	3		

Socioeconomic Class:

Low income groups were the predominant group (60.8 %) and were more significantly related to Primary enuresis.(P value < 0.05)

Table – 17 Socioeconomic status

	Low income	Not Low income	Significance	
			χ^2	P
Primary	29	12	4.217	***0.0400***
Secondary	2	6		

The results of Monosymptomatic versus Non Monosymptomatic Enuresis are tabulated below.

Table – 18 Mono Vs. Non-Mono Symptomatic Enuretics

	Mono symptomatic Enuresis (%) n = 7	Non Mono symptomatic Enuresis (%) n = 33	Probability P
Males	5 (71.42)	21 (63.63)	0.2776
Females	2 (28.58)	15 (36.37)	
Diificult to arouse	4 (57.14)	18 (54.54)	0.9007
Low specific Gravity	6 (85.71)	18 (54.54)	0.1346
Spina bifida	4 (57.14)	13 (39.39)	0.3936
Low Bladder capacity	5 (71.42)	16 (48.48)	0.2766
Family History	4 (57.14)	15 (36.37)	0.3147

The above table shows that there are no statistically significant variations between monosymptomatic and nonmonosymptomatic enuretics as far as the risk factors are considered.

Discussion & Analysis

Enuresis is common among younger children and its frequency decreases with increasing age. The prevalence of Enuresis among 5 – 12 year olds is reported as between 1.4 to 28 % in most studies.

Primary enuresis formed 84 % of cases while secondary 16%.This was similar to already reported case series.

Table 19 Comparison of studies for proportion of Primary Enuresis

Author & Country	N	Proportion of Primary Enuresis
Iduoriyekemwen et al, Nigeria[16]	64	94%
Murat Unalacak et al, Turkey[17]	111	75.7%
A.Bourquia et al,Morocco[18]	532	91.5%
Present study	51	84 %

Since the present study is a Hospital based study, the age at presentation does not reflect the true prevalence. The mean age at presentation of 8.75 years is similar to Robson et al[19] whose study is also a similar hospital based study.

In the present study we see more children in the older age group than community based studies. This could be because of the fact that, this is a hospital based study and parents in general don't view enuresis a problem in younger children and seek medical attention only if it persists for long.

Table 20 Age Distribution

Age Group	All Case n=51 (%)	Primary n= 43(%)	Secondary n= 8(%)	Significance	
				χ^2	P value
5-7 yrs	19 (37.3)	17 (39.5)	2 (25)	3.001	0.2230
8-10 yrs	19 (37.3)	17 (39.5)	2 (25)		
11-12 yrs	13 (25.4)	9 (21)	4 (50)		

Males have a higher prevalence than females but the present study shows at least in the lower age groups the presentation is almost the same.

Table 21 Age versus Sex Distribution

Age Group	All Case n=51 (%)	Male n= 30(%)	Female n= 21(%)	Significance	
				χ^2	P value
5-7 yrs	19 (37.3)	9(30)	10 (47.6)	2.794	0.2473
8-10 yrs	19 (37.3)	11(36.67)	8 (38.1)		
11-12 yrs	13 (25.4)	10 (33.33)	3 (14.3)		

Day time symptoms

Day time symptoms were observed in 88.2 % of patients which was comparable to the study done by Robson et al[19] where daytime symptoms were found in 84.1 % of patients. This reinforces the fact that the term “nocturnal” may be misleading and a thorough history may be needed to ascertain daytime symptoms.

Family History

Family history of enuresis was present in 41.2 % of children. This was comparable to Ozden et al[20] who showed a positive family history in 44.9 % of children (n = 105). But there is wide variation in family history as illustrated in the table below.

Table 22 Comparison of Family History Prevalence in various studies

Author	N	Family History (%)
Ozden et al, Turkey	105	44.9
Ali Gunes et al,Turkey[21]	84	32.14
Ferrara et al,Italy[7]	108	73.3
Praveen Kumar et al,India[22]	48	16.67
Present Study	51	41.2

Spina Bifida

Spina bifida was present in 37.25% of patients in the present study. This is comparable to the data by Praveen Kumar et al[22] who described 37% i.e. 18 of their 48 patients had spina bifida and is significantly higher than the general incidence in the population of 17.3 % reported by Boone et al[23]. (t=3.524, DF = 702, P =0.005).

Depth of sleep /Difficulty in Arousability

Difficulty in arousability was found in 52% of patients. Wide variation is found among literature. This may be because of various parameters/ scales used to assess arousability. Most studies however conclude that enuretics are deep sleepers.

Table 23 Comparison of Depth of Sleep in various studies

Author	N	Difficult to arouse/ Deep sleep (%)
Ferrara et al. Italy[7]	108	81.5
Ozden et al, Turkey[20]	141	60.2
Murat Unalacak et al, Turkey[17]	111	64.9
Present study	51	52

Bladder Capacity

Small Bladder capacity was present in 51 % of patients in the present study. Though there are many reports including one by Esperanca & Gerrard[10] way back in 1969 stating about low bladder capacity in enuretics, there are no studies showing the proportion of enuretics with low bladder capacity particularly using frequency – volume charts.

Socioeconomic Status

Low income was found to be associated in 60.78 % of children. But review of literature shows conflicting reports about association of socio-economic status with enuresis.

Table 24 Comparison of studies on Socioeconomic status

Author	N	Low income/Poor SE status (%)
Unalacak et al,Turkey[17]	111	50.5
Iduoriyekemwen et al, Nigeria[16]	64	70.3
Issa Hazza et al, Jordan[24]	162	67.3
Ali Gunes et al ,Turkey[21]	84	39.3
Present Study	51	60.78

This may be due to the demographic factors in the sampling of patients. In the present study the low income group is higher as our hospital is a government Hospital catering mainly to such sections of the society.

The rate of other risk factors such as sleep disordered breathing, Constipation, Documented UTI and post void residual urine is very low in our study precluding any meaningful comparison with older studies.

Comparison of Primary versus secondary Enuresis :

Primary and secondary enuresis have generally been considered to be separate entities with a different pathogenesis. For Most patients with primary enuresis the pathogenesis is considered to be related to the problem with arousal, overproduction of urine at night, a small nocturnal bladder capacity, or a combination of these factors. The common reported causes of SNE include UTI, constipation, urge syndrome/dysfunctional voiding, psychological stress, diabetes, and obstructive sleep apnea. A total of 43 (84.3 %) of the patients whom we assessed had PNE. This proportion is similar to that observed in other studies.

The major significant differences between the patients whom we report with Primary Enuresis and those with Secondary Enuresis are storage symptoms, cystitis symptoms and sleep disordered breathing which were more common in secondary enuresis ($P < 0.05$) and Low income which was more significantly associated with primary enuresis ($P < 0.05$).

There was no significant difference between patients with PNE and SNE when they were compared for symptoms of bladder over activity, Low

specific gravity, family History, Low bladder capacity or spina Bifida.

There was close similarity in the clinical presentations of the 2 groups. The common presence of daytime voiding symptoms in patients with both PNE and SNE suggests that daytime voiding habits might influence the attainment of nighttime continence.

The similarities in Primary and Secondary enuresis are also reflected in the study by Robson et al[19] who concluded that they likely share a common pathogenesis.

Comparison of Monosymptomatic versus Nonmonosymptomatic Enuresis:

Though the recent ICCS terminology differentiates these two there was no significant difference between Monosymptomatic and Non Monosymptomatic Enuresis.

This suggests that they may be part of the spectrum of the same disorder with slightly different presentation.

There are no previous studies differentiating the two groups to compare the present findings.

Limitations

One limitation of this study is the low number of patients. Despite the small sample size, 4 statistically significant factors that differentiate Secondary Enuresis from Primary Enuresis were identified.

Another limitation of this study is the selection of patients from a referral centre (Tertiary care Hospital) rather than from primary care level /community. The selection bias from relying on a referral practice to accumulate sufficient numbers of children with enuresis may be unavoidable.

This study is a preliminary investigation. Consequently, the power of our negative findings is limited. Larger controlled community based studies are needed to establish the findings.

Conclusions

Enuresis is a common illness of childhood and is often neglected and thought of as a developmental milestone to be achieved.

Though Enuresis is a single disorder and at times has a single symptom, the causation is multifactorial and these factors have to be kept in mind while deciding treatment.

Primary and Secondary Enuresis show many similarities in presentation while the few differences present show the difference in causes for secondary enuresis.

Monosymptomatic and Non Monosymptomatic Enuresis have no differences in the presentation and probably represent the spectrum of a same disorder.

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Abbreviations

ADH	-	Anti Diuretic Hormone
ICCS	-	International Children's continence society
MNE	-	Monosymptomatic Nocturnal Enuresis
NMNE	-	Non Monosymptomatic Nocturnal Enuresis
OAB	-	Over Active Bladder
PNE	-	Primary Nocturnal Enuresis
SDB	-	Sleep Disordered Breathing
SE	-	Secondary Enuresis
UTI	-	Urinary Tract Infection

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நேரம்	6-8	8 – 10	10 – 12	12- 2	2- 4	4 – 6	6- 8	8- 10	10 – 12
அளவு (மி.லி)									

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(8 மணிக்கு மேல்) ஞாயிறு :
இரவில் படுக்கையில் எத்தனை முறை சிறுநீர் கழித்தார் :

சனி :
ஞாயிறு :

KEY TO MASTER CHART

Name: Serial No:

Age: 1 (5-7 yrs)/ 2 (8-10 yrs)/ 3 (11-12 yrs)

Sex: 1 (male)/ 2 (female)

Educational Status of parents:

Father: 1 (Primary)/ 2 (Secondary)/ 3 (Higher Secondary)/ 4 (Graduate & Higher)/ 5 (Illiterate)

Mother: 1 (Primary)/ 2 (Secondary)/ 3 (Higher Secondary)/ 4 (Graduate & Higher)/ 5 (Illiterate)

Family Income : 1 (Low Income)/ 2 (Mod. Income)/ 3 (High Income)

Complaints:

Type of Enuresis (Primary): 1 (Primary)/ 2 (Secondary)

Type of Enuresis: 1 (Diurnal)/ 2 (Nocturnal)

Type of Primary Enuresis: 1 (Monosymptomatic)/ 2 (Non-Monosymptomatic)

Type of symptoms: 1 (Storage symptoms)/ 2 (Voiding symptoms)/ 3 (Bladder Overactivity)/ 4 (Cystitis)/5 (Others) / 6 (No)

Storage symptoms: 1 (Daytime frequency)/ 2 (Daytime incontinence)/ 3 (Nocturia) / 4 (No)

Voiding symptoms: 1 (Hesitancy)/ 2 (Weak stream)/ 3 (Intermittancy)/ 4 (No)

Overactive bladder symptoms: 1 (Urgency)/ 2 (Urge Incontinence)/ 3 (No)

Cystitis Symptoms : 1 (Dysuria)/ 2 (Foul smelling urine)/ 3 (Hematuria)/ 4 (Suprapubic pain)/ 5 (No)

Other symptoms: 1 (Holding maneuvers)/ 2 (Post micturition dribble)/3 (Genital/LUT pain)/ 5 (No)

Duration of sleep: 1 (<6 hrs)/ 2 (6-9 hrs)/ 3 (>9 hrs)

Arousablity of sleep: 1 (Easy)/ 2 (Moderate)/ 3 (Difficult)

Sleep disordered breathing: 1 (Yes)/ 2 (No)

Constipation: 1 (Yes)/ 2 (No)

Insults at home: 1 (Yes)/ 2 (No)

Insults at School: 1 (Yes)/ 2 (No)

Family History: 1 (Both parents)/ 2 (One parent)/ 3 (Sibling)/ 4 (Others)/ 5 (No)

Examination & Investigations:

External markers of spinal anomalies: 1 (Yes)/ 2 (No)

Urinalysis: 1 (Normal)/ 2 (Abnormal)

Urine Sp.Gravity: 1 (Low)/ 2 (Normal)/ 3 (High)

UTI by culture: 1 (Yes)/ 2 (No)

X ray LS Spine: 1 (L5)/ 2 (L5S1)/ 3 (S1)/ 4 (No)

USG Abdomen: 1 (Normal)/ 2 (Abnormal)

Renal Function: 1 (Normal)/ 2 (Abnormal)

Estimated Bladder Capacity: 1 (Low)/ 2 (Normal)/ 3 (High)

PROFORMA

NAME : AGE : SEX :

ADDRESS : EDUCATIONAL STATUS OF PARENTS :
FATHER :

MOTHER :

FAMILY INCOME :

COMPLAINTS :

HISTORY :

PRIMARY/SECONDARY :

IF SECONDARY, HOW LONG :

CONTINUOUS/ INTERMITTANT :

DAYTIME / NOCTURNAL :

STORAGE SYMPTOMS : YES / NO
IF YES TICK ANY OF THE FOLLOWING
: ↑ DAYTIME FREQUENCY/ DAYTIME
: INCONTINENCE/URGENCY/ NOCTURIA

VOIDING SYMPTOMS : YES / NO
IF YES TICK ANY OF THE FOLLOWING
: HESITANCY/ WEAK STREAM /
INTERMITTANCY

SYMPTOMS OF OVERACTIVE BLADDER : YES / NO
IF YES TICK ANY OF THE FOLLOWING
: URGENCY/ URGE INCONTINENCE

SYMPTOMS OF CYSTITIS / UTI : YES / NO
IF YES TICK ANY OF THE FOLLOWING
: DYSURIA / FOUL SMELLING URINE /
HEMATURIA/SUPRAPUBIC PAIN

OTHER SYMPTOMS : YES / NO
IF YES TICK ANY OF THE FOLLOWING
: HOLDING MANUVERS/ POSTMICTURITION
DRIBBLE /GENITAL & LUT PAIN

SLEEP HISTORY :
AVERAGE TIME OF SLEEP :

WHETHER GOOD SLEEPER OR NOT :

H/O SLEEP DISORDERED BREATHING : SNORING / MOUTH BREATHING/
↑ SLEEPINESS IN THE MORNING

DIET HISTORY :
FLUID INTAKE (AS PERCIEVED) : INCREASED / NORMAL/ DECREASED

CONSTIPATION : YES / NO

INSULTS AT SCHOOL (AS PERCEIVED BY THE CHILD) : YES / NO

INSULTS AT HOME (AS PERCEIVED BY THE CHILD) : YES / NO

DIFFICULTIES PERCEIVED BY THE PARENTS : YES / NO

FAMILY H/O ENURESIS : YES / NO
BOTH PARENTS : YES / NO
ONE PARENT : YES /NO
SIBLING : YES / NO
OTHERS : YES/ NO

EXAMINATION :

HEIGHT : cm PERCENTILE :

WEIGHT : kg PERCENTILE :

ANEMIA : YES / NO

BP :

EXTERNAL GENITALIA :

PER ABDOMEN :

RENAL ANGLE & SUPRAPUBIC FOSSA :

CNS EXAMINATION :

GAIT :
POWER :
TONE :
REFLEXES :
PLANTOR :
SENSORY SYSTEM :

LS SPINE EXAMINATION :

INSPECTION :
PALPATION :

INVESTIGATIONS :

URINALYSIS : ALBUMIN :
SUGAR :
DEPOSITS :

URINE SPECIFIC GRAVITY :

URINE CULTURE & SENSITIVITY :

XRAY LS SPINE :

USG ABDOMEN KUB :
PREVOIDING :
POST VOIDING :

UROFLOWMETRY :

URODYNAMIC STUDIES :

VCUG :

CT/ MRI LS SPINE :

RENAL FUNCTION TESTS UREA :

CREATININE :

OTHER INVESTIGATIONS :